

Amendments to the Specification

Please replace the paragraph beginning at page 1, line 13, with the following amended paragraph:

As it is well known that vision is established through sequential processes of ~~the~~ conversion of photostimulation received from an object by the eye into an electric energy; the resulting electric energy's transmission to the brain; and the brain's recognition and judgement of the color and shape of the object. Photostimulation received by the eye is converted into an electric energy in the retina, and when a photostimulation with a level exceeding the threshold of visual cell receptors is focused on the retina, a receptor potential is evoked in the optic nerve and then transmitted to the upper central nervous system in an impulse form. The retinal function of converting photostimulation into an electric energy is quite important for establishing vision. The retinal damage induced by injuries or diseases may result in visual disorders such as narrowing of visual field, reduction of visual acuity, and nyctalopia.

Please replace the paragraph beginning at page 1, line 28, with the following amended paragraph:

At present, in Japan, it is said there are millions of patients suffering from visual disorders such as narrowing of visual field caused by retinal disorders, reduction of visual acuity, and nyctalopia. The retinal disorders are mostly evoked by diseases such as retinitis pigmentosa, age-related macular degeneration, and diabetic retinopathy. For instance, referring to retinitis pigmentosa which is an intractable disease specified as a specific disease by the Ministry of Health, Labor and Welfare of Japan, congenital disposition deteriorates retinal cells to evoke visual field scotomas, and this results

in blindness after gradual progression. However, even when the retina is ~~suffered~~suffers from any disorder and, for example, ~~when in~~ retinitis pigmentosa ~~where in which~~ the damage only stays in visual cells so as to keep the optic nerve substantially normal conditions, artificial installation of devices for converting photostimulation into electric signals and transmitting them to the optic nerve would brighten the visual field, meaning that it would possibly improve "the quality of life".

Please replace the paragraph beginning at page 2, line 17, with the following amended paragraph:

Now, in this field, there have been energetically progressed researches on substituent materials for the retina such as "artificial retinae" where a photosensor, mainly composed of a photoelectric-converting device such as a charge-coupled device (CCD), is formed into a chip which is then embedded in the eyeball as disclosed, for example, in Japanese Patent Kohyo Nos. 511,697/96 and 506,662/99. Since conventionally proposed artificial retinae would have difficulties in miniaturizing both photosensors and external power supplies for actuating the photosensors, it is ~~estimable~~ clear that there still remain hurdles to be overcome until actual exploitation of a device that can be inserted into the eyeball for use.

Please replace the paragraph beginning at page 3, line 11, with the following amended paragraph:

The present inventors focused on organic dye compounds capable of absorbing ~~lights~~light (hereinafter designated as "light-absorbing organic dye compounds") and eagerly studied and screened them. As a result, they made a

novel finding that some of the light-absorbing organic dye compounds, including polymethine dyes, evoke receptor potential in response to photostimulation in animal optic nerves, particularly, their retinal nerve cells that constitute the optic nerve. They also found that an agent for evoking receptor potential, which comprises any of these light-absorbing organic dye compounds, can be advantageously used as a substituent material for vision-related substances, i.e., a substituent material for the retina.

Please replace the paragraph beginning at page 4, line 2, with the following amended paragraph:

The term "organic dye compounds" as referred to as in the present invention means organic dye compounds in general which evoke receptor potential in response to photostimulation in the optic nerve, particularly, those which have an absorption maximum wavelength in the visible region and evoke receptor potential in response to photostimulation in the optic nerve, particularly, retinal nerve cells which constitute the optic nerve when they receive visible lights. Any organic dye compounds with any structure can be arbitrarily used in the present invention as long as they absorb visible ~~lights~~light and evoke receptor potential in response to photostimulation in the optic nerve. Examples of such organic dye compounds are those which absorb ~~lights~~light in the blue, green and/or red regions in the visible region; acridine, azanulene, azo, anthraquinone, indigo, indanthlene, oxadine, xanthene, coumarin, dioxadine, thiazine, thioindigo, tetraporphyradine, triphenylmethane, triphenothiadine, naphthoquinone, phthalocyanine, benzoquinone, ~~benzopyrane~~benzopyran, benzofuranone, polymethine, porphyrin, and rhodamine organic dye compounds.

Please replace the paragraph beginning at page 4,
line 20, with the following amended paragraph:

Preferable ~~ones~~ among the above organic dye compounds are polymethine organic dye compounds such as oxanol, cyanine, styryl, merocyanine, and ~~redacyanine~~ rhodacyanine dyes, which are coupled with the same or different cyclic cores such as imidazole, indanedione, indolenine, oxazole, quinoline, selenazole, thiazoline, thiazole, thioxazolidone, thionaphtene, thiobarbituric acid, thiohydantoine, naphthoxazole, naphthoselenazole, naphthothiazole, pyrazolone, pyridine, benzimidazole, benzoindolenine, benzooxazole, bezoselenazole, benzothiazole, and rhodanine rings, comprising polymethine chains such as dimethine, trimethine, tetramethine, pentamethine, hexamethine, and heptamethine having (i) one or more substituents such as aliphatic hydrocarbon groups such as methyl, ethyl, propyl, and isopropyl groups; alicyclic hydrocarbon groups such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cyclohexenyl groups; aromatic hydrocarbon groups such as phenyl and biphenyl groups; and halogens such as fluoro, chloro, bromo, and iodine groups; and (ii) having at ~~their~~ both ends one or more groups of aliphatic hydrocarbon groups such as methyl, ethyl, propyl, isopropyl, 1-propenyl, 2-propenyl, butyl, isobutyl, sec-butyl, tert-butyl, 2-butenyl, 1,3-butadienyl, pentenyl, isopentyl, neopentyl, tert-pentyl, 1-methylpentyl, 2-methylpentyl, 2-pentenyl, hexyl, isohexyl groups; aliphatic hydrocarbon groups such as cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl groups; aromatic hydrocarbons such as phenyl group; ether groups such as methoxy, ethoxy, and propoxy groups; ester groups such as acetoxyl, benzyloxy, methoxycarbonyl, ethoxycarbonyl, and propoxycarbonyl groups; amino groups such as methyl amino, dimethyl amino, ethyl amino, diethyl amino, propyl amino,

dipropyl amino, butyl amino, and dibutyl amino groups; hydroxyl, carboxyl, sulfo, nitro, and cyano groups; and combinations thereof. Among these organic dye compounds, those which absorb ~~lights~~light in the blue, green and/or red regions ~~in the of~~ visible light are most preferably used. Examples of the counter ions in the polymethine organic dye compounds are selected, for example, from anions such as chlorine, bromine, and iodine ions; and cations such as ammonium, trimethyl ammonium, and triethyl ammonium ions, however, the polymethine organic dye compounds do not have any counter ion when they have a negatively or positively charged substituent intramolecularly.

Please replace the paragraph beginning at page 11, line 1 with the following amended paragraph:

All the above polymethine organic dye compounds can be obtained in the desired amount either by the method disclosed in "Kanko-Shikiso" (Photosynthetic Dyes), pp. 11-31, edited by Masaaki Hayami, published by Sangyo Tosho Publisher on October 17, 1997; or in accordance therewith. In case the compounds are commercially available, they can be optionally purified prior to use. ~~To evaluate~~Evaluation of whether organic dye compounds evoke receptor potential in response to photostimulation in the optic nerve can be determined in accordance with the intracellular calcium experiment method disclosed in "Jikken-Igaku" (Experimental Medicine), Vol. 7, No. 6, edited by Hideaki Karaki et al., published on April 5, 1989 by Yodosha, Co., Ltd., Tokyo, Japan, with a modification that ~~a testing an~~ organic dye compound ~~is coexisted~~to be tested coexists in animal retinal cells cultured in a nutrient culture medium containing a fluorescent calcium indicator, followed by detecting the intensity of fluorescence emitted from the indicator or of the electric potential generated intracellularly.

Please replace the paragraph beginning at page 13, line 4, with the following amended paragraph:

Examples of the above-identified former type of substituent materials for the retina are those which can be prepared by chemically binding a ligand specific to the receptor of retina to the organic dye compound(s), and injecting the resultant into the eyeball to allow the organic dye compound(s) to specifically bind to the surface of the retina, after being prepared into a in solution form. In this case, examples of such a ligand include visual-related substances, receptor proteins or antibodies against channel proteins, antibodies against receptor proteins, antibodies against membrane proteins, and fragments thereof.

Please replace the paragraph beginning at page 13, line 25, with the following amended paragraph:

The above biocompatible high molecules used as the base in the present invention are not specifically restricted as long as they have an adequate hydrophilicity/hydrophobicity, rigidity, and flexibility; have a substantial transparency through over the visible region; and have an adequate tolerance to wear-tear and *in vivo* enzymes. Examples of such biocompatible high molecules include those which are transplantable into the eyeball, for example, natural high molecules such as collagen, gelatin, cellulose, and hyaluronic acid; semisynthetic high molecules such as cross-linked products and derivatives of dextran, cellulose, pullulan, and heparin; synthetic high molecules including polymers and copolymers of silicon, polyacrylamide, polyacrylonitrile, polyacrylate, polyurea, polyurethane, polyester, polyethylene, polyethylene oxide, polyethylene glycol, polycarbonate, polycarbamate, poly(vinyl acetate), polyhydroxyalkylmethacrylate, poly(vinyl

alcohol), poly(vinyl pyrrolidone), and polymethacrylate; and complexes thereof. In the case of transplanting a base coupled with the organic dye compound(s) to the surface of the retina and when the retina inevitably contacts with the base's surface not coupled with the organic dye compound(s), the base should preferably be selected from electroconductive biocompatible-high-molecules.

Please replace the paragraph beginning at page 18, line 17, with the following amended paragraph:

When Fluo-4 acetoxymethyl ester is irradiated after being allowed to ~~up~~be taken up by nerve cells, it ~~shows a property of emitting a fluoreseence~~fluoresces at a wavelength of around 510 to 550 nm only when calcium ions flow into the nerve cells. Since it is well known that the induction of receptor potential in the optic nerve opens the calcium channels of cells and ~~allow~~allows calcium ions to flow into the cells, the fact that the intensity of fluorescence from Fluo-4 acetoxymethyl ester was increased only in the presence of any of the organic dye compounds, represented by Chemical Formulae 14 to 17, indicates that the compounds have a property of evoking receptor potential in response to photostimulation in the optic nerve. The above conclusion was also evidenced by the fact that a significant intracellular potential was observed in the absence of calcicludine.